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(54) **SMALL MOLECULES AND A PHARMACOPHORE MODEL FOR INHIBITION OF BOTULINUM TOXIN AND METHODS OF MAKING AND USING THEREOF**

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(58) **Field of Classification Search** 702/19; 703/11

See application file for complete search history.

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(57) **ABSTRACT**

Disclosed herein is a pharmacophore model for inhibiting Botulinum neurotoxin A metalloprotease activity which comprises a first plane A, a second plane B, a first hydrophobic moiety C, a second hydrophobic moiety D and a positive ionizable substituent E. The pharmacophore model may further comprise a heteroatom in the first plane A. In some embodiments, the distance between the center of the first plane A and the center of the second plane B is about 6.5 to about 9.5 Å. In some embodiments, the distance between the center of the first hydrophobic moiety C and the center of the second hydrophobic moiety D is about 8.0 to about 16.0 Å. In some embodiments, the distance between the center of the first plane to the center of the first hydrophobic moiety C is about 3.0 to about 5.0 Å. In some embodiments, the distance between the center of the second plane to the center of the second hydrophobic moiety C is about 3.0 to about 5.0 Å. In some embodiments, the distance between the center of the first plane to the center of the positive ionizable substituent is about 6.5 to about 9.5 Å.

17 Claims, 10 Drawing Sheets